

THE CONTROL OF TYPHOID FEVER BY VACCINATION.

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The discovery of the prevention of disease by the use of attenuated cultures of bacteria is due to Pasteur, who, in 1879, discovered that when a chicken was inoculated with a weakened culture of the chicken cholera bacillus it became sick but soon recovered and thereafter could resist injections with the virulent germ without injury. Following Pasteur's suggestion, those methods by which we protect against disease through the use of attenuated cultures are spoken of as "vaccination," and the materials "vaccines," in honor of Sir Edward Jenner, who discovered vaccination against small-pox. Pasteur's later success in immunizing animals against anthrax by similar methods led to experiments on laboratory animals looking toward immunization against typhoid fever.

In 1896, Doctor (now Sir) Almroth E. Wright inoculated two men with killed cultures of the typhoid germ. Pfeiffer and Kolle in the same year immunized two men and made a subsequent study of the changes produced in the blood. In 1897, Dr. Wright published the results of his inoculations made on eighteen men, which convinced him that the method was a practical one in the prevention of the disease. Dr. Wright soon after tried it in the British army in India, but the outbreak of the Boer War gave him his first opportunity to carry it out on a large scale. The results were hard to collect accurately and opinions differed greatly as to the ultimate success of the method. Dr. Wright, however, believed that the incidence of the disease was diminished about one half, and that the mortality was favorably influenced to even greater extent.

We now understand some of the reasons for the varying effect of the vaccine. At that time the cultures were heated to a temperature of 60° C. in order to destroy their vitality. It has since been

shown that this amount of heat injures or destroys to a great extent the power of the germs to produce a good response in the formation of those substances on which the body depends for its protection. At the present time the cultures are killed by heating to 53° C.

It was tried next on a large scale in the German Colonial army during the Hereros campaign of 1904-07. The reports of this expedition show that the percentage of typhoid fever among the uninoculated was almost 10 per cent., whereas among the vaccinated it was only a trifle over 5 per cent. Further than this, the figures show that 76.01 per cent. of the inoculated who contracted the disease had mild or moderately severe cases, with the fatal cases numbering 6.47 per cent., whereas only 61 per cent. of the uninoculated had light or moderately severe cases, while the mortality reached 12.80 per cent. It was further shown that among the vaccinated 60 per cent. of the fatal cases occurred in those who had received only one dose of vaccine, 33 per cent. in those who had received two doses, and only 8½ per cent. in men who had received the three inoculations (Russell).

The value of the method has been made the subject of study by a number of commissions appointed by various governments all of which have made favorable reports. After careful consideration, anti-typhoid vaccine was introduced in the United States army as a voluntary measure in 1909. The favorable results were so striking that in 1911 it was made compulsory for all officers and enlisted men under the age of forty-five years. The most striking example of its efficacy is afforded by a comparative study of two bodies of soldiers, approximately equal in numbers, living under similar conditions during the same period of the year, and in much the same climate, one stationed at Jacksonville, Fla., in 1898; the other at San Antonio, Tex., during the maneuvers of 1911. At Jacksonville there were 10,759 men, with 2,693 cases of illness known, or believed to be, typhoid fever, and 248 deaths. At San Antonio there were 12,801 soldiers with only one case of typhoid fever, which resulted in recovery. During the same time there occurred in the city of San Antonio forty-nine cases of typhoid fever with nineteen deaths, showing that the infection was prevalent in that community and demonstrating that the difference in the incidence of typhoid fever

was almost certainly due in large part to vaccination. As the troops had considerable freedom in visiting the city, this conclusion is rendered all the more certain.

PREPARATION OF THE VACCINE.

The method of preparation varies slightly in different laboratories, but the following is probably most often followed.

Pure cultures of the typhoid bacillus are grown on slanted agar, preferably in flat bottles, which give a large surface for culture. At the end of forty-eight hours the bacilli are scraped off and suspended in normal salt solution. The suspension is then heated for one hour to a temperature of 53° C., preferably in a water bath, after which it is standardized by comparing it with normal blood. Equal parts of normal human blood and the suspension of bacteria are mixed, and oftentimes diluted in order to facilitate counting. Spreads from the mixture are made on slides, stained, and a large number of fields (usually one hundred) examined, and both red blood cells and bacteria are counted. The average number of blood cells per field and the average number of bacteria per field are then compared. The normal blood count is taken at five million red cells for each cubic millimeter. Knowing this, it is easy to determine the number of germs per cubic centimeter. The vaccine is then diluted with normal salt solution until the mixture contains one thousand million bacilli per cubic centimeter. If it is to be sent out to physicians in general practice, it is better also to make a further dilution of the suspension to five hundred million per cubic centimeter for the first injection so that the size of the dose may be kept uniform while the number of bacteria contained in the dose is varied. The vaccine may be preserved for considerable lengths of time by the addition of one fourth per cent. of lysol, or carbolic acid. When kept in a cool and dark place its properties are maintained uninjured for at least three months.

It is also advised that the material should not be used until it is three weeks old, as freshly prepared vaccine apparently is more apt to give severe local reactions than that which is older.

POLYVALENT VACCINE.

At the present time many laboratories are using what is called polyvalent vaccine; that is, one made of a number of pure cultures derived from different sources, mixed together in approximately equal proportions. Thus, in preparing vaccine for the immunization of the French soldiers in Morocco cultures were obtained from cases of typhoid fever occurring in that country. Some bacteriologists also add to the vaccine cultures of the para-typhoids, A and B. At the Laboratory of Hygiene of the University of Wisconsin it is our invariable practice to prepare polyvalent vaccine.

Vincent, who has prepared most of the vaccine used in the French army, uses twelve different strains. After full growth has been obtained, the bacteria are autolized in salt solution with frequent shaking, and killed by being subjected to the action of sulphuric ether.

DOSAGE.

In America the dose universally employed is that advised by the army. Three doses are given ten days apart. The first dose consists of five hundred million bacteria, the second and third one thousand million each. The injections are made preferably in the upper arm about the insertion of the deltoid muscle, and are given under the skin and not into the muscles. The skin is sterilized with iodine, and the sterile needle is thrust through the area thus prepared. It is customary to vaccinate about four o'clock in the afternoon so that any reaction which takes place will occur during the night and be practically over with by the next day.

The use of alcohol in any form is prohibited, as even moderate amounts seem to increase the severity of both local and general symptoms.

No special precautions are necessary and the vaccine does not usually interfere with the ordinary vocations of life. Occasionally slight chilliness and even rigors may occur combined with headache, general malaise, and sometimes distinct nausea. Locally, there is an area of redness and tenderness, the worst of which is over with within twenty-four hours. Suppuration never occurs.

The vaccine is well borne by women and children, but the dose

for children should be smaller than that given to adults in proportion to their weight, the dose given being that proportion of the adult dose which the weight of the child bears to the average adult weight, namely, one hundred and fifty pounds.

Major Russell reports that of three hundred and fifty-nine children vaccinated in no case had any bad effects been observed, and no case of typhoid fever had occurred amongst them up to the time of his report. In approximately one hundred and twenty-nine thousands injections in adults there were only six tenths of one per cent. of severe reactions. Of these, three tenths of one per cent. followed the first injection.

The vaccine should not be given to anyone running a temperature. Vincent has shown that in persons suffering from malaria the occurrence of a paroxysm is oftentimes precipitated by the giving of a dose of vaccine. In the enormous practice in the United States army the only serious result which has been observed occurred in a man suffering from an unrecognized incipient tuberculosis. The rule, therefore, is to be sure that the person about to be inoculated has a normal temperature.

GENERAL APPLICATION OF THE METHOD.

It is evident that the use of vaccine is particularly applicable to armies or other large gatherings of men who are apt to be in temporary quarters deprived of the usual sanitary arrangements for the disposal of sewage. However, the use of the vaccine has a very much wider range than this, being of great value in the suppression of local epidemics. A typical case of its use under these circumstances will be mentioned.

A water borne epidemic occurred in Avignon, France, a town with a population of 49,000, in 1912. Six hundred and forty-four cases with sixty-four deaths were reported, but it is certain that the total number of cases reached 1,500. The garrison of the town consisted of 2,053 men. Of these, 1,366 were vaccinated; 687 not vaccinated. Among the unvaccinated there occurred 159 cases of typhoid fever with 21 deaths; while not a single case occurred amongst those who had been vaccinated. All lived under the same

conditions, drank the same water, ate the same food, and did the same work.

In the State of Wisconsin, the bacteriologist of the State Laboratory of Hygiene has administered the vaccine in two outbreaks, one occurring in a county hospital, and the other in a small village. At the institution one hundred and six persons were vaccinated. One case of typhoid fever occurred amongst those who received the vaccine, but within such a short time that it was evident that the person had been infected before vaccination was practiced. The case was atypical and of the mildest type, resulting in recovery, showing that the vaccine exercises a favorable effect when given during the period of incubation. During an epidemic in the town of Warrens, Wis., one hundred and sixteen persons were vaccinated. The epidemic ceased at once, and since that time only one case of typhoid fever has been reported among the vaccinated.

The method is of the greatest use in institutions, especially hospitals. It has long been known that nurses were more liable to typhoid fever than other people, as the result of direct exposure.

Dr. Spooner began the inoculation of nurses in the Massachusetts General Hospital, and reported that for the first time in the history of the institution no nurses had suffered from typhoid fever during the year. The practice has, since October, 1912, been extended by him to twenty-three hospitals in Massachusetts. In all, 1,361 individuals have been treated. In the same hospitals there have been six hundred and seventy-four persons exposed but not vaccinated. Among the vaccinated there have been three cases of typhoid and para-typhoid fever. Among the uninoculated there have been seventeen cases of typhoid and para-typhoid fever. It is evident that a large amount of protection was furnished by the inoculation among those especially exposed to the disease.

In the State of Wisconsin we advise that whenever a case of typhoid fever occurs in a family the other members of the family shall receive the protective inoculations. It is impossible to give exact figures of the results, but several very striking instances have been reported to us.

In Watertown vaccination was advised for the husband of a woman suffering from typhoid, and two trained nurses who were in attendance. One of the nurses refused to be vaccinated, saying that she was immune. About three weeks after leaving the case she went down with a severe case of typhoid fever, and was ill for several weeks. The husband and other nurse remained well.

The vaccination has been carried out also to a large extent in the National Guard of Wisconsin. This is still on a voluntary basis. In 1912 a large number of troops submitted to the inoculations, but many refused them. Some of those who declined were taken sick with typhoid fever soon after reaching home. We have not been able to trace any case among those who received the full vaccination.

Another condition in which the use of anti-typhoid vaccine is likely to prove of great service is in the treatment of typhoid bacillus carriers. During the last few years many cases have come to light in which individuals have been carrying the typhoid fever germ, and have been discharging it from their bodies for longer or shorter periods of time; such persons are known as "carriers." The most noted of these cases, "Typhoid Mary" in New York, is well known to the general public. Another striking example came to light on the steamship *Acme* sailing from San Francisco. So many cases of typhoid fever occurred among the sailors on this vessel that she obtained a bad name as the "fever ship," and it was difficult to secure good crews. The treatment of such cases has been a puzzle to the medical profession, and it seemed impossible to keep these persons in hospitals or under quarantine indefinitely. It has been found, however, in a number of cases such as those reported by Brem, and by Currie and McKeon, that the bacilli rapidly disappeared from the discharges of the body after administration of a vaccine made from the particular strain of typhoid germs recovered from the patient—what is known as an autogenous vaccine.

There are nineteen cases of carriers recorded in literature that have been treated with typhoid vaccine. Fourteen of these were successful; five were failures, though two of the latter were helped for a time.

In conclusion, I think we are justified in saying that in anti-typhoid vaccination we have an efficient method for the control of the disease under many and varying circumstances. It can never, however, take the place of sanitation, the proper disposal of sewage, and provision of safe water supplies.

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